Mouse Models for Stem Cell Therapeutic Development

Grant Award Details

Mouse Models for Stem Cell Therapeutic Development

Grant Type: Early Translational I

Grant Number: TR1-01232

Project Objective: Develop standardized mouse models for diabetes, Parkinson's,stroke, MI and traumatic brain injury for distribution to Investigators

Investigator:

Name:	Pali Kaur
Institution:	Jackson Labs
Type:	PI

Award Value: $3,759,134

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: Mouse Models for Stem Cell Therapeutic Development

Public Abstract:

Stem cells have tremendous potential for treating human diseases, as they have the unique capacity to develop into any cell type in the body and to proliferate indefinitely. The development of new therapies based on the transplantation of human stem cells (HuSC) into patients is a major focus of California researchers. A critical step prior to making new HuSC-based therapies available for use in humans is to test their safety and treatment efficacy in research animals that have the relevant disease. The laboratory mouse, widely recognized as the premier mammalian model for studying human disease, is the optimal organism for these preclinical studies. Mice naturally develop many important human diseases, and certain other diseases that afflict humans but normally do not occur in mice can be experimentally induced. While numerous valuable mouse models are currently available, these models must be further developed so that they can accept HuSC transplantation, through suppression of their immune systems. The lack of proven mouse models in which the immune system has been suppressed is a major bottleneck in research to translate discoveries in basic stem cell research to use in the clinic. An additional factor contributing to this bottleneck is a lack of efficient access to mouse models in general. Currently, mouse models are made available from individual laboratories as funds and timelines permit, and, additionally, the mice are generally not bred in quantities or under health conditions suitable for widespread distribution. The recent development at [REDACTED] of immune-deficient mice that support long-term transplantation with HuSCs opens a novel avenue for eliminating the bottleneck of inadequate animal models for preclinical stem-cell studies. At [REDACTED], we will use these immune-deficient strains together with the most valuable existing mouse models of disease to develop a broad array of immune-deficient mouse models of disease. We will also use state-of-the-art facilities to characterize biological traits in these models so that disease progression and the biological response to therapeutic compounds can be accurately assessed. Finally, we will establish and implement mouse production processes for efficient delivery of the desired quantities of mice to California stem cell investigators. It is critically important for CIRM investigators to have the appropriate mouse models to successfully advance therapeutics through the drug development pathway. Overall, this project will significantly accelerate the availability of effective, safe HuSC-based therapies to patients in California and elsewhere.

Statement of Benefit to California:

Stem cells, with their unique capacities to give rise to any cell type and to proliferate indefinitely, have enormous potential for treating human disease. Millions of Californians suffer from the diseases that could be treated effectively through therapies based on transplantation with human stem cells (HuSC). Before HuSC therapies are used in human patients, it is critical to test the safety and efficacy of the therapies using a research animal that has the relevant disease. The laboratory mouse is widely recognized as the most valuable animal model for studying human disease, and reliable mouse models for most of the major human diseases are currently available. However, these models have normal immune systems and are therefore not well suited for testing HuSC therapies, as the immune system recognizes the transplanted stem cells as foreign and attacks them. The lack of mouse models of disease in which the immune system has been suppressed significantly hinders the efforts of investigators in California and elsewhere to develop new HuSC-based disease therapies. An additional impediment is the lack of efficient access to the quantities of mice required for such studies, and to mice whose health, reproducibility, and research effectiveness has been assured. In the proposed project at [REDACTED], we will develop multiple state-of-the-art, immune-deficient mouse models of human disease that can be used for testing HuSC therapies, and we will establish the production processes for making these models readily available to California researchers. This project will benefit Californians by providing broad access to these critical models in the shortest possible timeframe. Further, this project leverages [REDACTED] resident expertise in creating new mouse models and its own investment in state-of-the-art animal production facilities in [REDACTED], allowing California to limit its investment in this type of critical, but costly, infrastructure.

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